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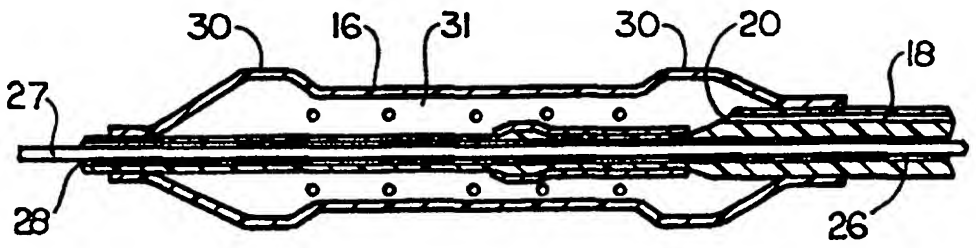

(57) Abstract

A method, and an apparatus for use in practicing the method, are provided by which a highly concentrated medication or chemotherapeutic agent can be applied locally under sufficient pressure to cause the medication or agent to penetrate into localized tissue or a body lumen. The total volume of medication or agent is quite small, well below levels that might cause an adverse reaction in other parts of the body. The catheter includes a thin wall flexible balloon having two collars and a central region between the collars, when the central regions defines a plurality of regularly spaced minute perforations through which medication may weep at a controlled, low flow rate. The flow rate is controlled by the minute perforations and the diameter of the central region is less than the diameter of the collars. In practicing the method of the invention, the balloon is selected such that the inflated diameter of the collars will correspond to or be slightly greater than the diameter of lumen into which the balloon is placed, and the central region will be slightly less than that lumen diameter, thereby defining a distinct, annular medication reservoir between the balloon and body lumen. The depth of the reservoir reduces the risk of medicine jetting against the vessel lumen if excess pressure is applied. Inflation of the balloon with a medication will cause the medication to weep from the central region of the balloon, consequently filling the reservoir and bathing the lumen walls. After a predetermined time, a sufficient amount of medication will be absorbed by the lumen walls and the balloon will be deflated so that the catheter may be withdrawn from the lumen. The quantity of medication that ultimately flows into the vessel lumen is sufficiently small so as to not cause any other systemic damage to the patient.

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BALLOON CATHETER FOR DRUG APPLICATION

Field of the Invention

The invention relates to catheter techniques for localized treatment, with medicine, drugs, or the like, of a blood vessel or other body organ having a catheter-receptive lumen.

Background of the Invention

In the treatment of various diseases, it is often desirable to treat a body organ, blood vessel or the like, with medicine or drugs in a high concentration. In some applications, the systemic application of a sufficiently high dose to treat the organ may flood the body with dangerously high levels of the medicament. For example, in percutaneous transluminal angioplasty procedures by which an obstructed portion of an artery is expanded to restore blood flow through the artery, there is a relatively high rate of restenosis (of the order of 30%) after performing the initial angioplasty. It has been reported that a significant contributing factor to restenosis may be smooth muscle cell proliferation of the artery wall. See "Intimal Proliferation of the Smooth Muscle Cells as an Explanation for Recurrent Coronary Artery Stenosis after Percutaneous Transluminal Coronary Angioplasty" by Garth E. Austin, et al, General American College of Cardiology, vol. 6, no. 2, August, 1985, pp. 369-375. It also has been reported that in animals the infusion of very high concentrations of heparin (or a particular component of heparin) tends to inhibit smooth muscle cell proliferation. See "Inhibition of Rat Arterial Smooth Muscle Cell Proliferation by Heparin" by John R. Guyton, et al, Circulation Research, vol. 46, no. 5, May, 1980, pp. 625-633; and "Vascular Smooth Muscle Proliferation Following Balloon Injury is Synergistically Inhibited by Low Molecular Weight Heparin and Hydrocortisone," John V. Gordon, et al, Circulation 76; IV-213, 1987. Thus, it may be advantageous to apply locally concentrated doses of heparin directly to an arterial wall that has been treated with angioplasty since locally effective doses of the heparin could be dangerous if introduced into the general circulation.

Although the desirability of applying high doses of medication to a local region of an artery or other blood vessel has been recognized (see U.S. Patent No. 4,824,436 to Wolinsky, et al, and U.S. Patent No. 4,423,725 to Baran), there remains the need for an improved catheter that

effectively delivers such high concentrations of medicine to an artery without also further traumatizing the arterial wall.

There have been attempts in the prior art to provide a balloon catheter that delivers high concentrations of medication to a localized area. One such type of balloon catheter shown, for example, in U.S. Patent No. 5,087,244 to Wolinsky et al., tends to force the medication into the arterial walls. The catheter shown in Wolinsky includes a shaft having a balloon secured near its distal end. The balloon has a central porous region and non-porous end regions. The diameter of the artery-contacting portion of the balloon is uniform, including both the porous central region and the non-porous regions. When the balloon is inflated, both the end regions and the central region directly contact the arterial wall. Such direct arterial contact can aggravate the trauma to an artery, which may have previously been traumatized by an angioplasty procedure. It is nevertheless intended that medicine consequently "weep" out of the minute pores in the central region and be infused into the arterial walls. The arterial walls, however, may have a sealing effect upon the pores which can tend to increase the impedance to the flow of medicine through the pores. Such increased impedance may demand an increase in the pressure that is applied to the medicine to cause it to flow through the pores and out of the balloon. If this increased pressure is higher than the recommended pressure for that catheter, the medicine might have a tendency to jet out of the perforations in the balloon in relatively high pressure streams that can cause focal tissue injury to the already traumatized artery.

Another balloon catheter design tends to "bathe" the arterial wall with medicine at relatively low pressures as embodied, for example, in U.S. Patent No. 4,636,195 (Wolinsky). The catheter shown in the Wolinsky '195 patent has two independent, longitudinally spaced balloons mounted on the distal region of the catheter shaft. Each of the balloons provides a substantial fluid seal against the arterial lumen to substantially seal off a specified region of the artery. The balloons are in communication with an inflation lumen which is dedicated solely to inflating the two balloons. A second lumen for fluid infusion also is provided through the catheter shaft and leads to a relatively large infusion hole between the balloons. When in use, the balloons are inflated and medication or other fluid is forced under pressure through the infusion lumen to the relatively large infusion hole. Any blood that might be trapped between the balloons and the artery should leak out of that region since the inflation of the sealing balloons can be controlled and can be expected to permit some leakage. A reservoir of fluid forms between the catheter and the arterial wall, thus bathing the treated area. Since this catheter

requires at least two lumens plus a third guidewire lumen, it necessarily appears that the overall diameter of the catheter is relatively large, thus limiting the catheter's use to larger diameter arteries.

Another catheter used to bathe a local arterial region with medicament is shown in Fig. 7 of PCT International Application No. PCT/US91/04288 (Shapland et al), which discloses a balloon catheter having a single balloon mounted near its distal end. The balloon has two lobes that are inflatable by a single lumen, and a drug supply lumen that extends along the side of the catheter shaft and through one of the lobes, terminating at a single, relatively large infusion hole. The catheter has a relatively narrow central region between the lobes that appears to have a diameter of just larger than the shaft of the catheter. This narrow central region could create a significant resistance in deflating the distal lobe, thus potentially complicating removal of the catheter from the artery. In addition, the Shapland balloon catheter requires at least three lumens (similar to the catheter shown in the Wolinsky '195 patent), thus making it difficult to incorporate into small diameter catheters.

It is therefore among the general objects of the invention to provide an improved method and low profile apparatus for delivering high concentrations of medications to a localized area of a wide range of diameters of body lumens, and to apply such medications under lower pressures while minimizing device contact with the arterial walls and associated arterial trauma.

Summary of the Invention

The invention involves a balloon catheter having a flexible cylindrical balloon at its distal end for delivering a fluid to a localized area of a body lumen. The balloon may be considered as being shaped to define two collars, a central region between the collars, and a plurality of regularly spaced minute perforations in the central region, through which medication may flow under conditions that reduce the tendency to jet yet which bathes the luminal surface and reduces the risk of trauma. A flow area defined by the perforations in the balloon is selected to provide a relatively low flow rate (typically on the order of a few cubic centimeters per minute) through the balloon wall. The flow rate should not be large enough so that the medication jets from the balloon when a maximum recommended pressure is applied to the interior of the balloon. The flow area of the perforation is sufficiently small enough so that it does not adversely impair the collapsing of the balloon upon aspiration, and also so that it prevents substantial medicine leakage through the perforations as the balloon is being inflated. The diameter of the central

region of the balloon is slightly less than the diameter of the collars to reduce the risk of jetting while effecting a low pressure bathing of the vessel wall and maintaining a large flow area through the entire balloon to facilitate rapid deflation. The balloon interior communicates with an inflation lumen that extends through the shaft of the catheter from a fitting at the proximal end of the catheter. The fitting is used for communicating the inflation lumen with a syringe or other pressure infusion device.

Prior to use, the catheter is selected with respect to the body lumen to be treated so that the inflated central region of the balloon will not be in contact with the body lumen, and the two collars of the balloon will be in substantial sealing contact with the body lumen. The substantial seal between the body lumen and the two collars enables fluids to slowly leak around the edges of the collars. Thus, when the balloon is inflated within the body lumen, the collars will press firmly against the surface of the body lumen, and the central region of the balloon will define a shallow annular reservoir between the balloon and the body lumen. Only a portion of the surface area of the balloon is therefore in contact with the arterial wall, thus minimizing arterial trauma. Once the balloon has been inflated with the medication solution, continued pressure applied to the interior of the balloon by the pressure infusion device will cause the medication to slowly flow through the perforations in the central region of the balloon. The medication will consequently fill the reservoir, thus bathing and eventually becoming absorbed by the walls of the body lumen. The reservoir is kept full while the medication is maintained under pressure, thereby continually providing medication to the reservoir as it is absorbed into the walls of the artery and as it leaks out around the edges of the collars. The continued pressure applied to the medication additionally may gently force the medication into the walls of the tissue defining the body lumen. Any jetting that might occur, if higher than recommended pressure is applied to the inside of the balloon may be minimized since the pores are submerged in the annular reservoir and do not contact the arterial wall. The collars tend to isolate the treated section of the body lumen by providing a substantial fluid seal in that area. Medication flow through the minute perforations can be maintained for up to several minutes to allow the medication a sufficient amount of time to penetrate the tissue to the extent desired without introducing large quantities of the medication into the patient's system. Withdrawal of the catheter is facilitated because the diameter of the central region is sufficiently large enough so that both shoulders will essentially simultaneously deflate under aspiration.

It is therefore among the objects of the invention to provide an apparatus and method for local treatment of a body lumen or vessel with a high concentration of medication or drugs, without exposing other parts of the body to such high concentrations of the medication or drug.

It is also an object of the invention to provide a catheter having a perforated balloon adapted to permit fluid to flow through the balloon wall at a low flow rate that is no greater than a predetermined maximum rate.

It is another object of the invention to provide a catheter having a perforated balloon that has a central drug delivery region that does not contact the inner walls of the body lumen.

It is also an object of the invention to provide an apparatus and method for local treatment of a body lumen with a high concentration of medicine or drugs in a manner that reduces the risk of trauma to the inner wall of the body lumen.

It is a further object of the invention to provide localized medication delivery to a body lumen at relatively low pressures.

It is yet another object of the invention to provide a low profile balloon catheter for local treatment of a body lumen.

It is still another object of the invention to provide a porous balloon catheter for local medicinal fluid treatment of a body lumen that minimizes the effects of jetting.

Description of the Drawings

The foregoing and other objects and advantages will be appreciated more fully from the following further description thereof, with reference to the accompanying drawings wherein:

Fig. 1 is a fragmented illustration of the balloon catheter used in the practice of the invention;

Fig. 2 is an enlarged longitudinal cross-sectional illustration of the distal end and balloon of the catheter;

Fig. 2A is an enlarged cross-sectional illustration of the catheter shaft taken along line 2A-2A of Fig. 1;

Fig. 3 is an illustration of the balloon laid flat showing the locations of the holes as they may be formed by a laser;

Fig. 4 is a side view of the flattened balloon as seen from an end of the balloon;

Fig. 5 is a sectional illustration through the balloon illustrating the circumferential spacing of the rows of holes;

Fig. 6 is an illustration of the balloon in a deflated condition prior to insertion of the balloon into a patient's artery;

Fig. 7 is an enlarged illustration of the balloon portion of the catheter in an artery and in an inflated configuration; and

Fig. 8 is an enlarged cross-sectional illustration of the boundary region of the balloon, fluid reservoir, and artery.

Description of the Illustrative Embodiment

Fig. 1 illustrates the catheter used in the practice of the invention. The catheter includes an elongated flexible shaft 10 that may be formed in an extrusion process from an appropriate polymeric material such as polyethylene. By way of example, when the catheter is intended to be used in the coronary arteries, the shaft 10 may be of the order of 150 cm long and may have an outer diameter of between 0.039 inches and 0.052 inches. The catheter has a proximal end 12 and a distal end 14. A bifurcate molding 13 is positioned near its proximal end to connect the lumens in the shaft 10 with separate proximal tubes 15, 17. An inflatable and deflatable balloon, indicated generally at 16, is mounted on the distal end 14 of the catheter shaft 10. As shown in Figs. 2 and 2A, the catheter shaft 10 includes an inflation lumen 18 that extends from the proximal end of the shaft 10 and terminates at an opening 20 within the balloon 16. A fitting 22 on the proximal end of the tube 17 may be connected to a syringe (not shown) or other pressure fluid delivery device to enable inflation and deflation of the balloon. The catheter shaft 10 also may be formed to include a guidewire lumen 26 that extends to and terminates in an outlet orifice 28 at the distal tip of the catheter shaft 10. The guidewire lumen 26, accessible through a fitting 24 on the proximal tube 15, is receptive to a guidewire 27 by which the catheter may be guided through a patient's vasculature to the site to be treated. In an illustrative embodiment, a catheter shaft 10 having a diameter of about 0.044 inches, may have a guidewire lumen 26 diameter of about 0.020 inches, and the inflation lumen 18 may have a maximum cross-sectional dimension of about 0.014 inches. Although side-by-side parallel lumens are shown in the drawings, other two lumen structures may be used, including a coaxial lumen structure.

As illustrated in Fig. 2, the balloon 16 is formed to have two collars 30 and a central region 31 between the collars 30. The diameter of the center region 31 of the balloon 16,

although less than the diameter of each of the collars 30 of the balloon 16, should be large enough so that both of the collars 30 inflate and deflate substantially uniformly when a pressure differential is applied to the inflation lumen 18. As an example, the central region 31 may have a diameter of 2.0 millimeters while the collars 30 each may have a diameter of 2.5 millimeters, thus defining a thin, but distinct, annular reservoir about the central region when the balloon is inflated inside a body lumen. The diameter of the central region 31 preferably is selected so that when inflated, it is spaced from the arterial wall to avoid or minimize any appreciable jetting effects against the arterial wall that may result from applying a pressure that is greater than the recommended maximum pressure for the catheter (about five bars). The length of the balloon 16 may be varied depending upon the size of the region to be treated.

The central region 31 of the balloon 16 is provided with a plurality of minute holes 29 that may be substantially regularly spaced about the balloon 16 (see Fig. 3). For example, it has been found that an array of between ten and forty holes 29 (preferably about twenty), each having a diameter of about twenty-five microns will perform satisfactorily. The holes 29 may be formed by a laser beam from an excimer laser having a wavelength of 248 or 308 nm. Holes so formed have been found to form clean edged holes 29 in the balloon material. Figs. 2 and 3 illustrate a satisfactory pattern of holes 29 including four longitudinally extending rows having five holes in each row. Some of the rows may be staggered longitudinally with respect to each other. The holes 29 are formed before the balloon 16 is attached to the catheter shaft 10. In forming the holes 29, the balloon 16 is laid flat, as shown in Figs. 3 and 4, while a laser beam is used to drill the holes 29 in the desired pattern. The aggregate flow area defined by the holes 29 is selected so that under the general recommended range of inflation pressures expected (between about one to five bars), the liquid flow through the holes 29 will be relatively low and will not exceed a predetermined maximum flow rate. The maximum flow rate should be selected so that the liquid will not jet through the holes 29. Although the foregoing configuration of holes 29 is believed to be satisfactory for possibly most, if not all, medications or drugs to be delivered, it is possible that certain medications or drugs may have viscosity and flow characteristics that would require modification to the holes 29. The foregoing array of holes 29 has been found to produce satisfactorily low flow rates of fluid medications having a viscosity and fluid characteristic similar to saline (such as a heparin solution). In accordance with the invention, the maximum flow rate may be between 2 to 12 cc per minute under inflation pressures on the order of two to five atmospheres. Additionally, it is important that the holes 29 do not define a relatively large

flow area that could adversely affect the rapidity with which the balloon 16 could be collapsed. Too large a flow area could compromise a physician's ability to withdraw the balloon 16 from the patient's vasculature. The flow area also must be small enough so that significant amounts of fluid will not flow from the balloon 16 prior to its being fully inflated. Such premature flow could undesirably introduce high concentrated medicine into the patient's general circulation.

The balloon 16 may be formed from various polymeric materials, such as polyethylene terephthalate, and preferably has a thin (0.001 inches or less), flexible, relatively inelastic wall. The balloon 16 may be fabricated as described in U.S. Patent No. 4,490,421 (Levy) or European Patent Application No. 88300025 (Saab), published July 13, 1988 (European Publication No. 274411), now abandoned, the disclosures of which are incorporated by reference herein, in their entities. By way of example, a catheter adapted for use in the coronary arteries may have a balloon 16 that is about twenty millimeters or more long with a wall thickness of 0.001 inches or less. It is contemplated that with a relatively inelastic balloon 16, several different sizes of (inflated) balloons 16 may be required, depending upon the application in which the catheter is to be used.

Passive perfusion holes 33 may be formed in the catheter shaft in connection with the guidewire lumen 26, adjacent each end of the balloon 16, to provide a path for blood to flow through the catheter while the balloon is inflated. This enables a physician to prolong the medicine delivery procedure because blood flow through the artery is not unduly interrupted. The guidewire 27 may be withdrawn from that portion of the guidewire lumen 26 (i.e. the area between the two perfusion holes 33) so that it does not impede blood flow through the lumen 26.

Use of the catheter and practice of the method may be illustrated through its use as an adjunct to an arterial angioplasty procedure, such as percutaneous transluminal coronary angioplasty. Typically, the angioplasty procedure will have been performed by the physician according to any of a variety of techniques using various angioplasty catheters available. For purposes of illustration, it may be assumed that the angioplasty procedure will have been performed either by a balloon catheter, laser catheter, atherectomy catheter, or other angioplasty catheter, that enlarges the lumen at the stenosed region of the artery to a nominal diameter of 2.5 mm. The arterial wall may display a certain amount of recoil after the angioplasty so that the actual luminal diameter may be slightly smaller than 2.5 mm. In order thereafter to treat the arterial wall with concentrated heparin (or an isolated heparin fraction having anti-proliferative effect), the angioplasty catheter must be removed from the patient while the guidewire 27

remains in place. The physician's assistant will have prepared the catheter of the present invention by filling the inflation lumen 18 and interior of the balloon 16 with a medication to purge the inflation lumen 18 and balloon 16 system of air. The balloon 16 will then be wrapped about the catheter shaft and collapsed to a low profile, as suggested by Fig. 6, so that it may be passed through an indwelling guiding catheter. The catheter 10 preferably is provided with one or more radiopaque marker bands by which the balloon 16 position may be monitored under fluoroscopy to verify placement of the balloon in the region to be treated. Once the balloon 16 is positioned at the site of the angioplasty, the syringe or other inflation device is operated to pressurize the inflation lumen 18 and interior of the balloon 16 to cause the balloon 16 to inflate as suggested in Fig. 7. By proper selection of the balloon size, the central region 31 of the balloon 16 will inflate into close proximity with the inner surface of the arterial lumen without actually contacting it, while the collars 30 will inflate into close pressing contact with the inner surface of the lumen to effect a substantial seal on each side of the central region. Pressure is applied continually by the inflation device (which may be fitted with a pressure gauge) to maintain a substantially constant pressure level as desired, a range of pressures anticipated being of the order of one to five bars. This pressure inflates the balloon 16 so that the collars 30 are firmly in contact with the luminal surface of the artery and the central region 31 is proximate to, but not contacting, the arterial wall. A shallow annular reservoir 34 thus is defined between the balloon 16 and arterial wall. Medication will then flow through the holes 29 in the balloon 16 and fill the reservoir 34, consequently bathing the arterial wall. The pressure and flow will be continued for a predetermined time, for example one to several minutes, or enough time for the medicine to sufficiently penetrate into the arterial walls. It should be noted that since the contact between the collars 30 and the artery may tend to cause the artery to flex, and also since the inner surface of the artery usually is not uniformly smooth or circular, the collars 30 may not provide a perfect fluid seal for reservoir 34. Blood that may be trapped in the reservoir 34 due to inflation of the balloon 16 should therefore migrate out of the reservoir 34, as will excess medication that flows from the balloon 16. After the medicine application process is completed, the balloon 16 is then deflated by aspirating through the inflation lumen 18 to cause the balloon 16 to collapse. The selection of the number of holes 29 and their size should be made to prevent the aspiration of appreciable amounts of blood from the artery into the deflating balloon. The flow area defined by the holes 29 is sufficiently minute and the balloon wall is sufficiently flexible so that the balloon 16 will readily collapse under aspiration. As previously suggested, the diameter of

the central region 31 is sufficiently large enough so that the two collars 30 should deflate simultaneously at substantially the same rate. After the balloon is deflated, the catheter is withdrawn from the patient.

Since the central region 31 of the balloon has a reduced diameter, there is less traumatic device contact with the arterial wall. If jetting should occur (when higher than recommended pressures are applied to the balloon), its effects may be avoided or minimized since the holes 29 are not in direct contact with the arterial walls. Accordingly, the invention is considered to provide a less traumatic localized medicine delivery than those catheters shown in the Wolinsky '244 patent. Moreover, the invention requires no more than two lumens and may have a lower profile than prior dual balloon devices. The invention is therefore capable of being used in smaller diameter arteries. Additionally, the diameter of the central region of the invention is selected so that both collars will deflate essentially simultaneously, thereby facilitating withdrawal of the catheter from the body lumen.

We have thus described the invention by which highly concentrated medication may be applied to a surface of a body lumen, such as an artery, under sufficient pressure to cause the medication to penetrate into the tissue without introducing excessively high volumes of the medication into the patient's general system. It should be understood, however, that although the invention has been described principally in connection with post-angioplasty treatment of an artery with heparin or an anti-proliferative fraction of heparin, the invention may be practiced in any instance where it is desired to apply a high concentration of medication to a local vessel or organ having a lumen accessible by a catheter. Thus, the invention may be used to deliver chemotherapeutic drugs in the treatment of cancer patients where it is desired to apply concentrated medication for chemotherapeutic agents to the diseased organ. The catheter may be passed into a lumen in the organ or may even be inserted into a lumen formed in the organ or tumor for the express purpose of receiving the catheter. Therefore, it should be understood that other embodiments, modifications and equivalents of the invention may be apparent to those skilled in the art without departing from its spirit.

Having thus described the invention, what we desire to claim and secure by Letters Patent is:

CLAIMS

1. A catheter for applying and maintaining a liquid against a surface of a lumen of a body vessel, comprising:

a supporting member adapted to be inserted into the lumen of the body vessel;

a flexible balloon mounted on the supporting member, the supporting member including an inflation lumen in communication with the interior of the balloon and having a portion adapted to be disposed outside of the patient;

the balloon having two collars and a central region between the collars;

the diameter of the central region of the balloon being less than the diameter of each of the collars of the balloon and also being sufficiently large enough such that the collars deflate substantially uniformly when a fluid pressure is applied to the inflation lumen;

the inflation lumen being in communication with both collars and the central region of the balloon;

the central region having a plurality of minute perforations adapted to provide a flow rate of said liquid, said flow rate being no greater than a predetermined maximum flow rate when the liquid in the balloon is under pressure;

the perforations defining a flow area sufficiently small so as not to adversely restrict the collapsing of the balloon about the support member under the influence of aspiration applied to the inflation lumen.

2. A catheter as defined in claim 1 wherein the collars have a diameter that is at least 0.5 mm larger than the diameter of the central region.

3. A catheter as defined in claim 1 wherein the predetermined maximum flow rate is selected so that the liquid will not jet through the perforations at all pressures up to and including a recommended maximum pressure.

4. A catheter as defined in claim 1 wherein the balloon has between about ten and forty minute perforations.

5. A catheter as defined in claim 1 wherein the perforations have a diameter of between 10 and 75 microns.

6. A catheter as defined in claim 1 wherein the apparatus is dimensioned and adapted to be percutaneously inserted and advanced into the coronary arteries.

7. A catheter as defined in claim 1 wherein the balloon has a wall having a thickness of no greater than about 0.001 inches.

8. A catheter as defined in claim 1 wherein the balloon is formed from polyethylene terephthalate.

9. A catheter as defined in claim 1 further including a guidewire lumen defining a first perfusion hole near the proximal side of the balloon and a second perfusion hole near the distal side of the balloon.

10. A catheter as defined in claim 1 wherein the two collars are free of perforations.

11. A catheter as defined in claim 1 wherein the liquid is heparin.

12. A catheter for applying and maintaining a liquid against a surface of a lumen of a body vessel, comprising:

an elongated flexible shaft having a proximal end and a distal end and having an inflation lumen extending from its proximal end toward its distal end;

a flexible balloon mounted proximate to the distal end of the supporting member, the interior of the balloon being in communication with the inflation lumen of the shaft, the balloon having two collars and a central region between the collars, the diameter of the central region of the balloon being less than the diameter of each of the collars of the balloon, the central region having a plurality of minute perforations adapted to provide a flow rate of said liquid, said flow rate being no greater than a predetermined maximum flow rate when the liquid in the balloon is under pressure;

the diameter of the central region and the diameter of the collars of the balloon being selected so that the central region does not contact the body vessel when the balloon is inflated.

13. A catheter as defined in claim 12 wherein the diameter of the central region is sufficiently large enough such that the collars deflate substantially uniformly when a pressure is applied to the inflation lumen.

14. A catheter as defined in claim 12 further including a guidewire lumen defining a first perfusion hole near the proximal side of the balloon, and a second perfusion hole near the distal side of the balloon.

15. A catheter as defined in claim 12 wherein the balloon defines a reservoir between the body vessel lumen and the balloon when the balloon is inflated inside the body vessel lumen.

16. A catheter as defined in claim 12 wherein the diameter of the central region and the diameter of the collars are selected so that the central region virtually contacts the lumen of the body vessel.

17. A method for causing a liquid to penetrate tissue defining a body lumen, comprising:

providing a catheter including an elongated flexible shaft having a proximal end and a distal end and having an inflation lumen extending from its proximal end toward its distal end; and a flexible balloon mounted proximate to the distal end of the supporting member, the interior of the balloon being in communication with the inflation lumen of the shaft, the balloon having two collars and a central region between the collars, the diameter of the central region of the balloon being less than the diameter of each of the collars of the balloon, the central region having a plurality of minute perforations adapted to provide a flow rate of said liquid, said flow rate being no greater than a predetermined maximum flow rate when the liquid in the balloon is under pressure;

inserting the catheter into the patient to position the balloon in the lumen;

inflating the balloon in the body lumen so that the collars of the balloon press in intimate contact against the inner surface of the body lumen to provide a substantial liquid seal, the

central region inflating to a diameter that is less than the diameter of the body lumen to define a liquid reservoir between the central region of the balloon and the inner surface of the body lumen;

maintaining a fluid pressure for a predetermined time to cause the liquid to flow out of the holes in the balloon and to fill the fluid reservoir; and

aspirating the balloon, after a predetermined time, to deflate the balloon and to remove the catheter.

18. The method as defined in claim 17 wherein the liquid is a concentrated medication and the pressure is not maintained for a period of time that would cause the maximum amount of medication tolerable by the patient to weep through the balloon perforations.

19. The method as defined in claim 17 wherein the body lumen is an artery and further comprising the additional step of performing an angioplasty in the artery prior to inserting the catheter into the patient.

20. The method as defined in claim 19 wherein the perforated balloon is inflated with a heparin solution.

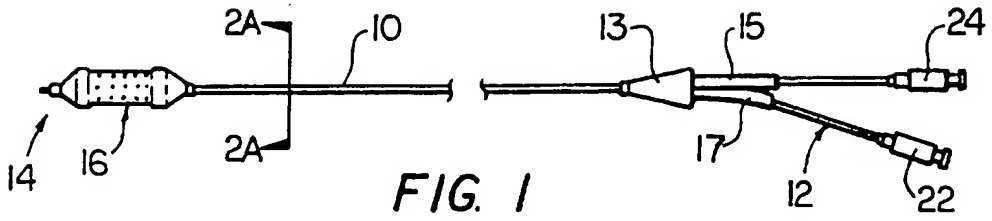

FIG. 1

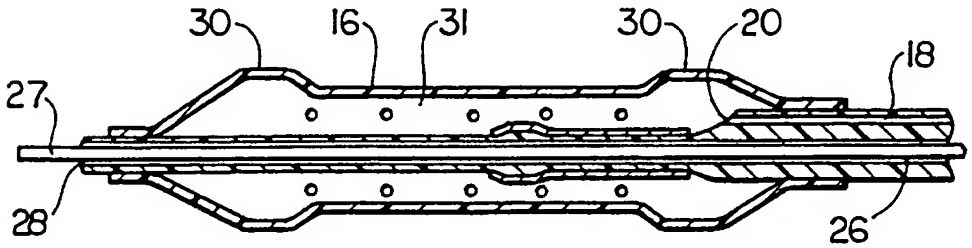

FIG. 2

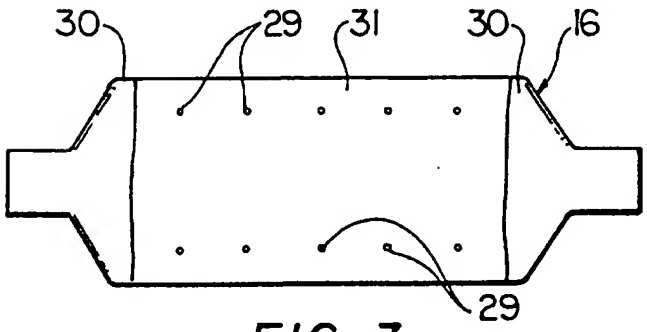

FIG. 3

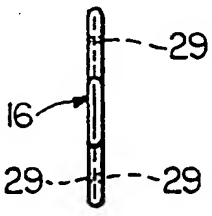

FIG. 4

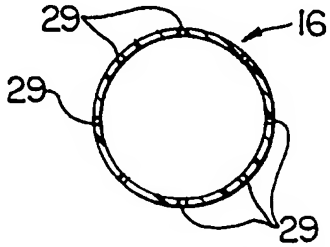

FIG. 5

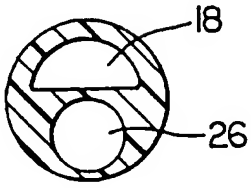

FIG. 2A

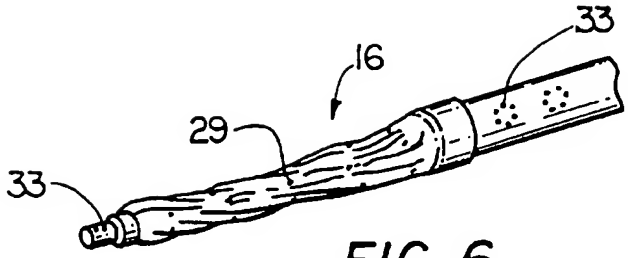

FIG. 6

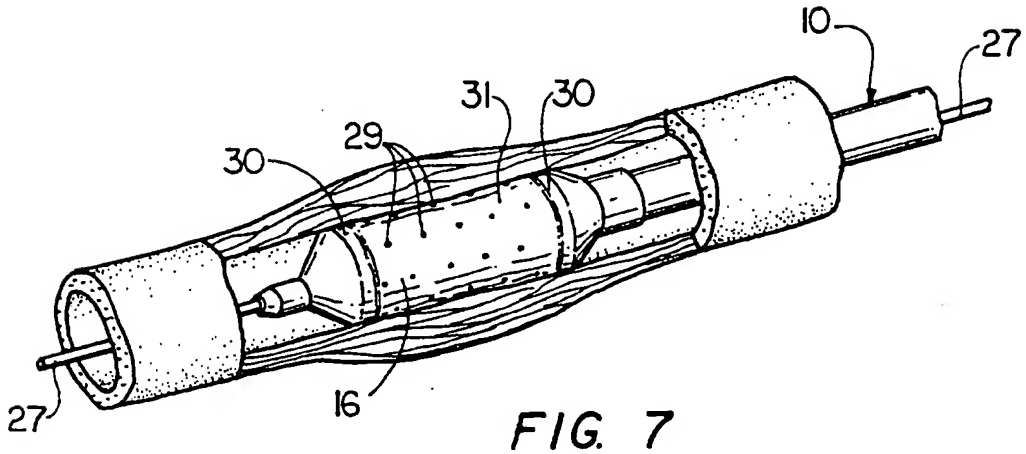

FIG. 7

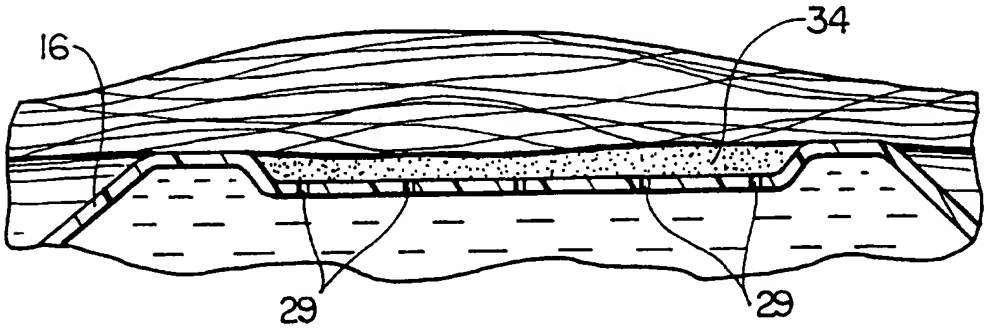

FIG. 8

INTERNATIONAL SEARCH REPORT

Inter. ...nal Application No
PCT/US 96/17434

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M25/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 318 531 A (LEONE) 7 June 1994 see abstract see column 1, line 51 - column 2, line 19 see column 4, line 8 - line 29; claims 1-3; figure 1 ---	1-16
A	EP 0 669 143 A (CARDIOVASCULAR DYNAMICS, INC.) 30 August 1995 see abstract see page 1, line 23 - line 42; claim 4; figures 1-4 -----	1-16

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search	Date of mailing of the international search report
28 February 1997	14.03.97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Michels, N

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 96/17434

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 17-20
because they relate to subject matter not required to be searched by this Authority, namely:
Please see Rule 39.1(iv) PCT
Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. .onal Application No
PCT/US 96/17434

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5318531 A	07-06-94	US 5213576 A	25-05-93
		US 5405472 A	11-04-95
EP 0669143 A	30-08-95	US 5470313 A	28-11-95
		JP 8052219 A	27-02-96